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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,443	02/10/2004	Gregory S. Bisacchi	HA0794 NP	9406

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,443	BISACCHI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10 and 21-27* is/are rejected.

7)☒ Claim(s) *1-5 and 11-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. According to paper filed on Aug. 15, 2005, the applicants have elected group II with traverse for further prosecution in response to restriction requirement.

2. Claims 1-27 are pending in the application.

Response to Arguments

3. Applicant's arguments filed on Aug. 15, 2005 regarding restriction requirement have been fully considered but they are not persuasive. The examiner does not agree with the applicants arguments that a serious burdon would not be imposed to search all different X groups. As stated clearly in the last office action, the compounds of groups I through X are structurally divergent, classified in different classes and subclasses and therefore, constitutes a burdensome search. Thus, restriction requirement as indicated is proper and thereby made final.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating thrombosis using instant compounds of formula (I) directed to the elected group, does not reasonably provide enablement for treating every known thromboembolic disorder, factor VIIa-associated disorder or pharmaceutical compositions comprising any other therapeutic agent besides instant compounds of formula (I) directed to the elected group. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, the state of the prior art, presence or absence of working examples and the breadth of claims.

The instant compounds are inhibitors of factor VII a as mentioned in the specification on page 46, second paragraph. The specification also teaches that factor VIIa is one of the precursors present in the blood for formation of thrombin which catalyzes the conversion of fibrinogen to fibrin, a key enzyme responsible for blood clotting (see page 1 of specification). Based on these teachings, the instant compounds will have utility in treating thrombosis. However, there is no teaching either in the specification or prior art references provided showing well known utility of factor VIIa inhibitors alone in every known thromboembolic disorder, factor VIIa-associated disorder or utility of combination of factor VIIa inhibitors with any other therapeutic agent for treating any disease or disorder. There is no teaching either in the specification or prior art regarding all known

disorders associated with factor VIIa and furthermore, whether these disorders are due to increased activity or decreased activity of factor VIIa etc. there are no working examples present showing efficacy of instant compounds in known animal models of every known thromboembolic disorder or disorders associated with factor VIIa. There is no teaching or guidance in the specification regarding effectiveness of combination of instant compounds with any other therapeutic agent in animal models of any disease condition. The instant compounds of formula (I) encompasses several hundreds of thopusands of compounds based on the values of variables R1-R3, W and X and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the effectiveness of instant compounds in animal models of every known thromboembolic disorder or disorders associated with factor VIIa following their in vivo administration and hence their utility for treating these disorders.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6-10, 21 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-10 recite the limitation "prodrug" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 10 recites the limitation "SO2alkyl or SO2(phenyl) for variable X"in claim 1. There is insufficient antecedent basis for this limitation in the claim.

In claim 21, the term ---thromboembolic disorder--- is indefinite since specific disorders are not defined.

In claims 24 and 25, the term ---other therapeutic agents selected from--- is indefinite since specific drugs are not defined.

In claim 26, the term---Factor VIIa-associated disorder---- is indefinite since specific disorders are not defined and furthermore, how are they asoociated with factor VIIa?

8. Claims 1-12 and 19-27 are objected for containing non-elected subject matter.

Allowable Subject Matter

9. The following is a statement of reasons for the indication of allowable subject matter: The instant compounds of formula (I) directed to the elected group, pharmaceutical composition containing these compounds and a method of treating thrombosis using these compounds are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the prior art, Ackermann (U.S. Patent 6,242,644, cited on applicant's form 1449) discloses N-(4-carbamimidoyl-phenyl)-glycine derivatives which are closely related to instant compounds. However, the closely related compounds (see compoundd of formula 1A in col. 4) disclosed by Ackermann differ from the instant compounds in having instant variable Z as phenyl group instead of an isoquinoline ring.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625